Remarks

The Amendments

Claims 1 and 2 have been amended to recite unbranched nucleosides at the positions of the nucleoside that are subject to selective desilylation. Support for the amendments can be found in, for example, Figures 2, 7, 8, 9, and 10, along with the corresponding Examples 4-7 on pages 83-86. This amendment is made in order to advance prosecution and is made without prejudice to prosecution of the unamended claims in a continuing application.

Rejection of Claims 1-26 Under 35 U.S.C. §112, second paragraph

Claims 1-26 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite. Applicants respectfully traverse the rejection.

The Office Action asserts that the phrase "selectively desilylating the product from (c)" renders all claims in which it appears indefinite. Applicants do not concede that the phrase "selectively desilylating the product from (c)" renders all claims in which it appears indefinite as the phrase operates to implicity describe the positions of the nucleoside that are subject to desilylation when Claim 1 and Claim 2 are read in their entirety. However, claims 1 and 2 has been amended such that the phrase "selectively desilylating the product from (c)" is now "selectively desilylating said 5',3'-cyclic silyl protecting group of the product from (c)". Therefore, Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-8, 11-18, and 24-26 Under 35 U.S.C. §102(b)

Claims 1-8, 11-18, and 24-26 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Tang *et al.* Applicants respectfully traverse the rejection.

Under 35 U.S.C. § 102, a claim is anticipated only if each and every element as set forth in the claim is found in a single art reference. *Verdegaal Bros. v. Union Oil Co.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); *In re Recombinant DNA Technology Patent and Contract Litigation*, 30 USPQ2d 1881, 1885 (S.D. Ind.1993) ("A patent is anticipated only if all the elements and limitations of the claims are found within a single, prior art reference."); *Structural Rubber Products Co. v. Park Rubber Co.*, 223 USPQ 1264, 1271 (Fed. Cir. 1984) (All elements of the claimed invention must be contained in a single prior art disclosure and must be arranged in the prior art disclosure as in the claimed invention); M.P.E.P § 2131. Furthermore, no difference may exist between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of invention. *In re Recombinant DNA Technology Patent and Contract Litigation*, 30 USPQ2d 1881, 1885 (S.D. Ind.1993). Also, the identical invention must be described or shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); M.P.E.P. § 2131.

The Office Action recognizes that Tang discloses a method for the synthesis of phosphoramidite derivatives of 2'-C-β-methyl cytidine, which is a branched nucleoside. The instant claims, however, recite methods for synthesizing **unbranched** 2'-O-silyl nucleosides. Tang does not teach or suggest the identical invention as set forth in the instant claims. Tang teaches the use of a method for the synthesis of phosphoramidite derivatives of 2'-C-β-methyl cytidine, which are substantially different compounds than phosphoramidite derivatives of cytidine by virtue of the 2'-C-methyl group that is present in 2'-C-β-methyl cytidine (branched) but not present in the ribonucleotides of the present invention (unbranched). Clearly, the 2'-C-β-methyl cytidine nucleoside of Tang is a

structurally distinct nucleoside than the nucleosides in the instant application which all lack a 2'-C-methly group. Additionally, Tang teaches that the chemical properties of the 2'-C-β-methyl cytidine are very different from that of a corresponding cytidine ribonucleotide. The fact that deprotection of the 2'-O-TBDMS group with tetrabutylammonium fluoride (TBAF) was shown to be dramatically slower for 2'-C-B-methylcytidine than for cytidine demonstrates that the presence of the 2'-C-methyl group alters the reactivity of 2'-O-silyl-2'-C-methyl toward silyl deprotection. In the case of a 2'-C-methyl cytidine trinucleotide, treatment with TBAF for 24 hours provided no deprotected product (Tang et al., 1999, J. Org. Chem., 64, p 750 and Figure 1), whereas the cytidine containing trinucleotide was almost completely desilylated during this time (Tang et al., 1999, J. Org. Chem., 64, p 750 and Figure 1). As such, because the 2'-O-TBDMS group remained intact on the 2'-O-TBDMS-2'-C-β-methyl cytidine but not the 2'-O-TBDMS cytidine nucleoside, one of skill in the art would not expect that selective deprotection as employed in the case of a 2'-branched nucleoside would work in the case of an unbranched nucleotide as is described and claimed in the instant invention.

Therefore, Tang does not teach or suggest the use of an identical method for the synthesis of a 2'-O-silyl-nucleoside phosphoramidite. Furthermore, differences exist between the claimed invention and Tang, as viewed by a person of ordinary skill in the art. Specifically, Tang does not teach or suggest an identical method for the synthesis of unbranched 2'-O-silyl-nucleoside phosphoramidites. The identical invention is not described or shown in as complete detail in Tang as is contained in the instant claims. As such, Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-45 Under 35 U.S.C. §103(a)

Claims 1-45 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Tang *et al.* in view of Usman *et al.* Applicants respectfully traverse the rejection.

The Office Action concedes that Tang teaches a method for the synthesis of phosphoramidite derivatives of 2'-C-β-methyl cytidine using only 2'-C-β-methyl cytidine as the nucleoside, but does not teach the protection of the nucleic base after 5', 3'-cyclic silyl protection of the nucleoside using t-Bu_2SiCl2 is introduced, or the introduction of a 2'-O-triisopropylsilyloxymethyl protecting group recited in the instant claims. The Office Action asserts that Usman teaches these missing elements.

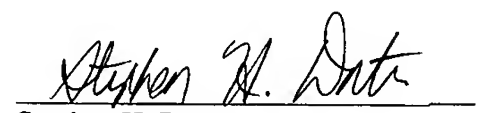
As discussed above, Tang only teaches the use of a branched nucleoside, 2'-C-β-methyl cytidine, as the nucleoside used in the synthesis of 2'-O-TBDMS-2'-C-β-methyl cytidine phosphoramidite derivatives. Tang teaches away from the instantly claimed invention. As described by Tang, the branched 2'-O-TBDMS-2'-C-β-methyl cytidine nucleoside was highly resistant to fluoride mediated deprotection compared to 2'-O-TBDMS cytidine, which is readily deprotected in the presence of fluoride ion. The structural and chemical differences between the branched 2'-C-β-methyl cytidine and unbranched cytidine nucleosides highlights the innovation provided by Applicant's invention. The branched 2'-C-β-methyl cytidine nucleoside is amenable to selective deprotection of a 5',3'-cyclic silyl protecting group because the 2'-O-silyl group is highly resistant to fluoride mediated cleavage. In fact, because Tang was not able to remove the 2'-O-TBDMS group from 2'-O-TBDMS-2'-C-β-methyl cytidine, Tang suggests using the 2'-O-tetrahydropyranyl ether as a protecting group rather than 2'-O-silyl protection in the case of 2'-C-branched nucleosides.

Based upon the teaching of Tang, one of skill in the art would not expect that selective deprotection of a 5',3'-cyclic silyl protecting group in the presence of a 2'-O-silyl protection group would work when using an unbranched nucleoside such as cytidine. Therefore, Tang does not teach or suggest using a 5',3'-cyclic silyl protecting group in the presence of a 2'-O-silyl protection group for the selective synthesis of unbranched 2'-O-silyl nucleosides. Usman also does not teach or suggest using a 5',3'-cyclic silyl protecting group in the presence of a 2'-O-silyl protection group for the selective synthesis of unbranched 2'-O-silyl nucleosides. Usman therefore does not remedy the deficiencies of the primary reference and a person skilled in the art would not be motivated to combine Usman with Tang. For these reasons, Applicants respectfully request withdrawal of the rejection.

Allowance of the claims and passage of the case to issue are respectfully solicited. Should the Examiner believe a discussion of this matter would be helpful, he is invited to telephone the undersigned at (312)-913-0001.

Respectfully submitted,

Dated: December 22, 2003

By: 

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